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A CONTRIBUTION TO THE PATHOLOGY OF EXPERIMENTAL DIPHTHERIA, WITH SPECIAL REFERENCE TO THE APPEARANCE OF SECONDARY FOCI IN THE INTERNAL ORGANS.

By A. C. Abbott, M. D., *First Assistant*, and A. A. Ghriskey, M. D., *Assistant in Bacteriology, Laboratory of Hygiene, University of Pennsylvania.*

(*From the Laboratory of Hygiene of the University of Pennsylvania. Read before the Johns Hopkins Hospital Medical Society, March 20th*, 1893.)

In the course of our studies upon the alterations produced by the bacillus diphtheriæ in the tissues of susceptible animals we have encountered upon several occasions a condition that, so far as we are aware, has either escaped notice or has not been mentioned by other writers upon this subject. In addition to the macroscopic alterations commonly observed in the experimental form of this disease, and the microscopic lesions described by Oertel[1] in the tissues of human beings dead of diphtheria, and by Welch and Flexner[2] in the tissues of animals that have succumbed to inoculation with the diphtheria virus, we have detected in seven autopsies a condition of the omentum that we propose to describe in this contribution.

The animals upon which the experiments were performed were guinea-pigs, and the cultures employed were but a few generations removed from undoubted cases of primary diphtheria.

The special lesions, which form the subject of this paper, consist in minute, yellowish, lens-shaped foci located in the omentum, usually between its peritoneal layers, and usually circumscribed in outline. When visible to the naked eye they are rarely larger than the eye of a small cambric needle, and of about the same shape. They are occasionally larger than this, but more commonly smaller, being frequently so small as to be detected only by microscopic examination of sections of the hardened and embedded omentum. As a rule the omentum containing these bodies is somewhat congested, and often presents a shriveled appearance at its free margin. It is in this free margin that the foci are most commonly to be found. Upon microscopic examination these nodules are seen to be sometimes very sharply circumscribed, while again they are slightly less regular in outline. At times they may be seen lying between folds of the peritoneum (Fig. 1), while again they will be limited by the walls of lymphatic spaces. Upon closer examination they are seen to consist of polynuclear

[1] Oertel: "Die Pathogenese der epidemischen Diphtherie. Nach ihrer histologischen Begründung." Mit Atlas. Vogel, Leipzig, 1887.

[2] Welch and Flexner: "The Histological Changes in Experimental Diphtheria." Johns Hopkins Hospital Bulletin, No. 15, August, 1891. Also, "The Histological Lesions produced by the Toxalbumen of Diphtheria," Ibid., No. 20, March, 1892.

leucocytes and those having the horseshoe-shaped nucleus, closely packed together. We have rarely detected any of the fixed tissue elements within these nodules. The majority of the leucocytes composing them contained bacteria which in their morphological and staining peculiarities were identical with the bacillus diphtheriæ.

In one instance in which there was an unusually large nodule we obtained from it the virulent diphtheria bacillus in pure culture; in the majority of cases, however, the nodules were so small and the danger of error during manipulation so great that we decided to rely upon microscopic examination for the identification of the bacteria within them.

The histological structure of these nodules is simple, and there is but little to describe beyond that which has already been mentioned, namely, that so far as we have been able to make out they are nothing more than masses of leucocytes, many of which are in the phagocytic condition, crowded together within the lymph channels of the omentum. At times they may be seen lying directly beneath one of the layers of the peritoneum, while again they may occupy lymph canals between the two layers where these are in juxtaposition. As a rule there is little or no reaction of the tissues about them, and they appear only as if the lymphatic space in which they are located had become plugged up by them.

In one case in which an unusually small amount of material had been injected into the animal, only two of these foci could be found, and these only upon microscopic examination of sections of the omentum. They were characteristic in their histological structure, but most careful search failed to reveal the presence of bacteria in either of them.

In a number of other cases that we have examined the omentum has been found congested and often diffusely infiltrated with leucocytes along and about the course of the vessels, but in none of these instances could we detect the circumscribed accumulations of leucocytes to which we are referring. It was also impossible for us to detect micro-organisms of any character by microscopic examination. In six cases in which the bacilli were present in the omentum they were always within the circumscribed nodules of leucocytes, either free or within the body of cells. In the majority of instances, so far as we can state from careful examination of the sections, they were within the bodies of phagocytes. In one case in which there was a slight peritonitis we found a few endothelial cells containing bacilli.

In our search for these nodules, after first having detected them, our attention was frequently attracted to small, whitish points in the omentum, which often led us to believe that the foci of leucocytes were present, but which, upon microscopic examination, proved to be minute lymphatic bodies, evidently rendered conspicuous through the action of the diphtheritic poison, an enlargement analogous to that seen in the grosser lymphatic structures when under the influence of this poison. In some of these lymphatic structures leucocytes could be detected, but in no instance have we found bacilli within them. In one instance a karyokinetic figure was observed.

The first three cases in which our attention had been attracted to these nodules were animals that had been inoculated subcutaneously. The inoculations were made in the tissues of the abdominal wall a little to the right of the median line and about midway between the free margin of the ribs and the inguinal region. In two of these animals fluid cultures were employed, while in the third a portion of a solid culture on Löffler's blood-serum mixture was used.

In our efforts to cause the reappearance of the omental nodules various methods of inoculation were employed. It was plain that the passage of the bacilli from the seat of inoculation in the abdominal walls to the omentum where they were found was by means of the lymph canals, the course being in all probability by way of the inguinal and retroperitoneal lymph glands, though microscopic examination of both of these structures failed to reveal the presence of bacilli within them. This opinion was strengthened by an experiment made by injecting into the same locality of another animal a small quantity of sterilized India ink. The animal was killed after 48 hours, and not only the inguinal and retroperitoneal glands were found to be pigmented, but the omentum as well, though in the case of the latter the pigmentation was not circumscribed and was not present in nodules similar to those seen in the cases in which cultures of the bacillus diphtheriæ had been used.

We tried superficial and deep injections, sometimes immediately beneath the skin, and again as nearly between the muscular layers and the peritoneum as possible without entering the latter, but no constancy in our results could be obtained, and it is impossible for us to say upon what factor the presence of the foci found in the omenta of these three cases depended. The tissues at the site of inoculation were examined microscopically, but nothing was found to aid us. There were several features, however, in addition to conditions mentioned by other observers,[1] that may be interesting to note, viz.: In a few sections made directly through the point at which the bacilli had been deposited we found, in addition to the hyaline condition of the muscle fibres, that there could, here and there, be detected a penetration of these degenerated tissues by the bacteria that were lodged in clumps in the lymphatic spaces adjacent to them—a condition that we have endeavored to represent in Plates 4, 5 and 6, and which is apparently identical with the condition of the muscle fibres described by Klein,[2] at the seat of inoculation of two cows into which bouillon cultures of the bacillus diphtheriæ had been introduced. We have failed, however, to detect the mycelial-like threads to which he makes reference, and have found only the long, irregularly staining forms that are common to blood-serum cultures of this organism. Sometimes the penetration would occur through the side of a fibre, as seen in cross section (Fig. 4), while again the bacilli grew in from one end (Fig. 5), or from both ends and the side (Fig. 6). It was also a common occurrence to find degenerated muscle fibres into which leucocytes had wandered. In the main, though, the local changes were the same as those given by others who have studied the process in detail.

[1] See Welch and Abbott: "The Etiology of Diphtheria," Johns Hopkins Hospital Bulletin, No. 11, February and March, 1891, p. 29.

[2] Klein: The Etiology of Diphtheria. Nineteenth Annual Report of the Local Government Board, 1889–90. Supplemental Report of the Medical Officer, pages 173 and 174.

From THE LABORATORY OF HYGIENE, UNIVERSITY OF PENNSYLVANIA.

Fig. 1

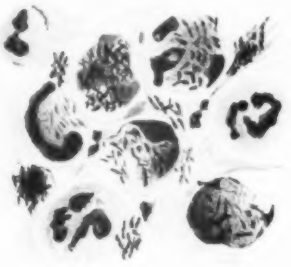

Fig. 2

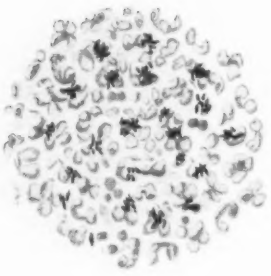

Fig. 3

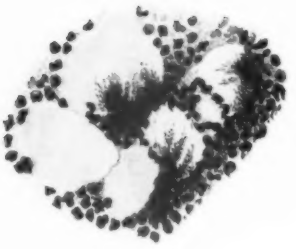

Fig. 4

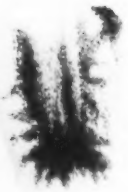

Fig. 5

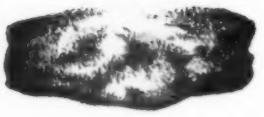

Fig. 6

A. C. ABBOTT, Del.

To accompany Dr. Abbott's Article, April Bulletin.

After failure to produce the omental foci in five out of eight cases, we abandoned the method of subcutaneous inoculation for one that we thought more promising in its outlook. Bearing in mind the fact that it is possible to inject in a fairly perfect way the lymphatic system of small animals through the testicle, this point was chosen for subsequent inoculations. Four animals were inoculated with either bouillon cultures or suspensions of the bacilli in physiological salt solution, by direct injection into the testicles. The results of these injections were satisfactory in each case; two of the animals that had received bouillon cultures, the one 0.6 cc., the other 0.7 cc., presented at autopsy most exquisite omental foci, in all respects identical with those present in the first three animals studied, except they were more numerous; while the remaining two animals, the one of which had received 0.4 cc. and the other 0.5 cc. of a salt solution suspension of the bacilli, presented the foci, but fewer in number and smaller in size. Those from the animal that had received 0.5 cc. were characteristic in histological structure, and contained bacilli which under Gram's method of staining showed the characteristic morphology of the bacillus diphtheriæ. The remaining animal had also foci in its omentum which were histologically identical with those seen in the other animals, but in which no bacteria could be detected. We cannot account for the absence of bacilli from the foci of leucocytes in this case.

A point of particular interest in connection with the cases in which the injections had been made into the testicle was the diminution of œdema of the superficial tissues and its increase in the tissues of the abdominal cavity. In two of these cases straw-colored fluid was not only found free in the peritoneal cavity, but the small intestine was practically filled with fluid and its walls were intensely œdematous; and in all four of these cases the œdema of the subcutaneous tissues over the point of inoculation was markedly diminished. In these cases also the retro-peritoneal lymph glands, particularly those on the side inoculated, show a marked reaction, and we felt reasonably sure of detecting the bacilli within them; but most careful microscopic search failed to reveal them in these tissues, though the omentum may have contained numerous foci of leucocytes and large numbers of bacilli. It is possible, however, that by culture methods we might have obtained them from these tissues, but we considered the possibility of error under these circumstances so great that only microscopic examination was thought safe.

The method of examination to which we have given the preference consists in staining the tissues lightly in a watery solution of Bismarck brown, and after carefully washing them out in alcohol to subject them to the method of Gram. If bacteria are present they appear in very striking contrast upon the brown background (see Fig. 3). If the Gram method is used alone or with eosin, as we have tried it, the possibility of error is great. The chromatin of the nuclei of the tissue cells frequently takes on and retains the violet stain, and portions of the nuclear beam-work may appear so like the bacillus diphtheriæ or clumps of this organism as to make the differentiation by this method very difficult. By the method that we have employed the nuclear network stains brown, and does not lose this color when subsequently treated with the violet dye. A very good idea of the contents of these nodules can also be formed by crushing one upon a cover-slip and manipulating it in the way commonly employed in making cover-slip preparations. A portion of one of the nodules treated in this way and stained in Löffler's blue is depicted in Fig. 2.

Until recently the opinion in regard to the relation of the diphtheria bacilli to the organism in which they are located has been, that they remained at the point at which they were found or had been deposited, but recently evidence has been presented that will cause some modification of this view.

Frosch,[1] in a series of bacteriological studies upon the cadavers of individuals dead of diphtheria, has detected the bacilli in the internal organs of ten out of fifteen cases examined by him at autopsy. He found them in the brain, lungs, liver, spleen, kidneys, cervical and bronchial glands, blood, and in the pericardial and pleural fluids. They were least frequently present in the liver; they were regularly to be found in pneumonic nodules, in the spleen, and in the bronchial and cervical lymph glands. In only one of the ten cases were they missed from the blood of the heart.

Through which channels the bacilli gain access to the internal organs in human diphtheria it is, in the present state of our knowledge, impossible to say, but that it is through the lymphatics, and largely through the aid of the wandering phagocytic cells, that they appear as secondary depositions in the experimental forms of the disease, we think our observations just cited leave but little doubt.

We have had no evidence in our cases to lead us to suppose that the migration occurs through the vascular system. On the contrary, in those omenta that were congested and more or less diffusely infiltrated with leucocytes, particularly along the course of the vessels, we have not succeeded in detecting the bacilli either free or in phagocytes in a single case, whereas, on the other hand, in the cases in which they did appear in the omentum it was, as stated, only where the phagocytes were densely packed within the lumen of a lymph canal, or in connective tissue spaces between or beneath the peritoneum.

Description of Plate.

Fig. 1. Section through focus of leucocytes located in the omentum between the layers of the peritoneum. Leitz, obj. 3, ocular I, tube 160 mm.

Fig. 2. Contents of one of the foci dried upon a cover-slip and stained with Löffler's blue. Leitz, o. i. $\frac{1}{12}$, ocular III, tube 160 mm.

Fig. 3. Section of one of the foci that had been hardened in absolute alcohol, stained with Bismarck brown and subsequently by Gram's method. Leitz, o. i. $\frac{1}{12}$, ocular III, tube 160 mm.

Figs. 4, 5, 6. Hyaline muscle fibres from seat of inoculation, showing penetration of bacilli into them. Stained with eosin and methylene blue. Leitz, obj. 7, ocular III, tube 160 mm.

[1] Frosch: Verbreitung des Diphtherie-bacillus im Körper des Menschen. Zeit. f. Hygiene u. Infectionskrankheiten, 1893, Band XIII, p. 49-52.

DIPHTHERIA WITH BRONCHO-PNEUMONIA.

By Simon Flexner, M. D., *Associate in Pathology, Johns Hopkins University and Hospital.*

The contribution which I have to make to this subject is based upon the examination of two cases of diphtheria in human beings in which the smaller bronchi were invaded by the diphtheria bacillus. The fact that the diphtheria bacilli are taken up, in these examples of Dr. Abbott, by leucocytes is borne out also by the results obtained in at least one of the cases to which I refer. This case has been presented to the society before, so that nothing at this time need be said concerning the gross anatomical features. As I mentioned then, cultures made from the lung proved the diphtheria bacillus to be one of the micro-organisms present. Our idea at that time was that the organisms were not actually derived from the parenchyma of the lungs, but it was probable that we had entered a small bronchus which we knew had been invaded by the diphtheria bacilli, since a typical diphtheritic membrane could be made out in all the smaller bronchi. We realized that it would require a histological examination of the tissues to prove whether or not the diphtheria bacilli were actually present in them.

In the second case, the diphtheria bacilli were not found in cultures made from the lung. There were broncho-pneumonic areas in the lungs of both cases, and in these the micrococcus lanceolatus was obtained from the nodules.

The publication to which Dr. Abbott has referred made us still more interested in determining whether or not the diphtheria bacilli were present in these areas in the lungs. Up to the present time, on account of circumstances over which I have had no control, the complete study of these two cases has been impossible. Still I have been able to cut sections from various parts of the lung, from the areas of broncho-pneumonia and elsewhere, and from the larger bronchi near the root of the lung and the trachea, and I can say this much that the diphtheria bacilli are present in the smaller bronchi which are found in these areas of broncho-pneumonia, and that they are there not alone in the membrane but also in the exudate which fills the bronchi. This exudate consists almost entirely of polynuclear leucocytes, and the protoplasm of these leucocytes is crowded with diphtheria bacilli. Some time was spent in searching for bacilli in the broncho-pneumonic areas. In two instances I felt quite sure that I had found isolated diphtheria bacilli in them, but they were not there in large numbers. It may prove, on further examination, that they are more common. They are certainly much less numerous than the micrococci lanceolati, which are present in considerable numbers.

With regard to the phagocytic action of the leucocytes in reference to the bacillus diphtheriæ, it was observed by Dr. Welch and myself that not infrequently when the bacilli were injected beneath the skin the leucocytes took up some of them. In some instances these leucocytes preserved their normal appearance, while in others they appeared to be injured, the nucleus being destroyed or fragmented and the cells dead.

I have made some experiments relating to the production of a pseudo-membrane in which were used dead diphtheria bacilli alone, and also dead bacilli which had been combined with the filtrate from a bouillon culture of the diphtheria bacillus. I found that if I injected the dead diphtheria bacilli alone a small nodule formed at the site of injection, which, after a day or two, shrunk in size and finally disappeared. But if the dead diphtheria bacilli were injected along with a filtrate from a bouillon culture, the animal would die in consequence of the action of the diphtheritic virus. The dead bacilli gave rise then to a nodule, and on cutting sections of this nodule we found that the dead bacilli had been taken up by the leucocytes and presented much the same appearance under the microscope as the specimens which Dr. Abbott exhibits.

ACUTE ULCERATIVE ENDOCARDITIS DUE TO THE BACILLUS DIPHTHERIÆ.

By W. T. Howard, Jr., M. D.

The history in brief was that of a man, a Russian Pole, æt. 44 years, married, a laborer, who was admitted to St. Joseph's Hospital, November 7th, 1892, in the service of Dr. F. A. Warner. He complained of weakness, pain in the head, and diarrhœa. His previous history had been good. His present illness began on November 1st, with a chill, high fever, pain in the head, abdomen and limbs; nausea, vomiting and diarrhœa. The man remained in this state for seventeen days; his temperature running an irregular course, his pulse at first was of good volume and under 90 beats per minute, but towards the last was very weak and rapid. He died in collapse.

His heart, which I show here, is larger than normal. The myocardium is firm and rather pale. The coronary arteries appear normal. On the upper or auricular aspect of the mitral valve there is situated a mottled red and white, irregular, granular-looking thrombus mass. This mass begins just below the base of the valve and completely covers both segments. Its greatest thickness is at the free border of the valve. The mass is everywhere intimately adherent to the underlying valve tissue, and varies in thickness from 0.2 to 1 cm. On removing portions of it with the finger the endocardium is found to be rough, ulcerated and hemorrhagic. On the under or ventricular surface of the posterior segment there are several smaller points of ulceration, which are in places covered with the same fibrinous material seen on the upper surface. The lower surface of the anterior segment is free from ulceration. When the surfaces of the thrombus

mass are brought together the auriculo-ventricular opening is almost completely closed. There are a few small vegetations on the ventricular surface of the aortic valve. The parietal endocardium is unchanged and the other valves are normal.

The liver was large and very much congested.

The spleen was very large, soft, and nearly the whole organ was the seat of an infarction. In the larger branches of the splenic artery there were white and red thrombus masses.

Both kidneys showed acute nephritis and were the seat of numerous infarctions.

Cover-slip preparations made from the thrombus mass on the mitral valve, and from the spleen and kidneys, all showed the presence of a bacillus with all the morphological characters of the bacillus diphtheriæ. This bacillus was the only organism present. Cultures were made on glycerine agar from the mitral valve, the lungs, the liver, spleen and kidneys.

In the tubes from all these sources were obtained in pure culture numerous colonies identical in appearance with colonies of the bacillus diphtheriæ. On the second day after the autopsy, cultures made from the heart thrombus were inoculated by Dr. Welch and myself into a rabbit and into a guinea pig. Neither of the animals died.

The bacillus has been studied by Dr. Welch, by myself and by several other workers in the laboratory here, and by Dr. Abbott in Philadelphia, and none of us has been able to make out any difference between this bacillus and the bacillus diphtheriæ, either morphologically or by culture methods. The only point of difference is that this bacillus has so far failed to kill animals.

For histological study of the process in the mitral valve I have made sections through the posterior segment, perpendicular to the surface. Beginning at the base of the valve, at its insertion, there is a loss of the endothelial cells of the endocardium. This is the first step in the process. Just above the thrombus mass here there is a large area over which the endothelial cells are lost. Here also there is a considerable local reaction, shown by a proliferation of the fixed cells of the part and by an infiltration of the tissue by a large number of polynuclear leucocytes. Just at the edge and on the surface of the valve there are great numbers of bacilli in the exudation. The bacilli do not penetrate the tissue to any distance, and are not seen deeper than the first two or three rows of cells.

Immediately below this area the thrombus mass commences, and, under the low power, several different appearances are met with. The mass in sections stained with eosin and methylene-blue is seen to be made up of different layers. On the free surface there is a thick layer composed of myriads of these bacilli; beneath this is a layer of fibrin, very poor in cells. Scattered about in this fibrinous mass are large and small clumps of bacilli. The bacilli here are usually placed in long, thick bands, but may be seen in smaller scattered masses. At the point of junction between the endocardium and the thrombus mass the endothelial cells are entirely lost, and at this place there is a dense line of bacilli. The endothelial cells cannot be made out at all. Beneath the layer of bacilli the muscle tissue of the valve is hyaline.

Very extensive and interesting changes, which we will not go into here, are shown in the kidneys. There are no areas of necrosis seen in the liver, although many bacilli can be made out in the capillaries.

Histological study shows that the bacillus concerned in the lesions present in this case is to a certain extent a pus producer. In certain areas in the mitral valve especially there is shown a considerable amount of local reaction. The hyaline degeneration noted in the muscle tissue of the valve is of particular interest.

The striking points in this case are a malignant endocarditis with general infection caused by a bacillus that is morphologically and by culture methods indistinguishable from the bacillus diphtheriæ.

For those interested I pass around for comparison cultures in various media of the organism found in this case and of the laboratory stock culture of the bacillus diphtheriæ. It will be seen that the two are identical.

Under the microscopes I have placed sections of the mitral valve showing the lesions and the bacilli described.

(This case will be reported in detail later.)

REMARKS BY DR. WELCH.

Dr. Abbott's observations that the bacillus diphtheriæ may produce lesions containing the bacilli at points distant from the seat of inoculation are interesting. It has been generally supposed that in experimental inoculations of guinea-pigs with this micro-organism, the bacilli develop only locally at and near the point of inoculation, and that they do not multiply in the internal organs and tissues distant from the inoculation. We must, in the light of these new observations, modify to some extent this view, but Dr. Abbott's results do not seem to me absolutely discordant with our previous conceptions. He was able to obtain the foci in the omentum containing bacilli after inoculation, both in the abdominal subcutaneous tissue and in the testicle, more regularly after the latter procedure. By the latter method especially the bacilli might pass directly along the lymph-channels to the peritoneum, as it is well known that the abdominal lymphatics can be readily filled with injecting fluid by injecting into the testicle, so that we may suppose that the bacilli are introduced into the peritoneum almost as directly as they are into the subcutaneous tissue by hypodermic inoculation. The same thing might happen, although less easily and frequently, by inoculation into the abdominal wall. I should be inclined therefore to attribute these omental foci to the direct and rapid penetration of the bacilli from the seat of inoculation to the peritoneum, so that the conditions for their production would not be so unlike those for the formation of the lesions near the point of inoculation. This view might be tested by determining whether the omental foci can be produced by inoculations in situations less directly connected by lymphatic channels with the peritoneum, than is the case with the testicle and the abdominal wall.

Dr. Flexner's communication is interesting, as showing the depth to which the bacilli can penetrate into the smallest bronchial tubes. It does not, however, subvert the current opinion that the complicating broncho-pneumonias of diphtheria are due to infection with other micro-organisms, the

streptococcus pyogenes most frequently, occasionally the micrococcus lanceolatus and other bacteria.

I have followed with exceptional interest the study of Dr. Howard's case of ulcerative endocarditis. We found in this case in pure culture and in large number in the valvular vegetations, the spleen and the kidney, a bacillus absolutely indistinguishable from the Klebs-Löffler bacillus of diphtheria in its morphological and cultural properties. The two organisms have been studied most carefully side by side in all sorts of culture media, and no distinction can be found between them. Dr. Howard's bacillus, however, is not pathogenic to guinea-pigs. Does this suffice to separate it as a distinct species from the genuine Klebs-Löffler bacillus? According to the investigations of Roux and Yersin, of Dr. Abbott and others, the genuine bacillus diphtheriæ may occur devoid of pathogenic properties in our animals used for experiment. If then we admit that Dr. Howard's bacillus is in reality the bacillus diphtheriæ, we have the first recorded observation of a case of ulcerative endocarditis due to this organism, and we are reminded of the old name for this affection, diphtheritic endocarditis, a name based, however, on anatomical rather than etiological reasons.

PERITONITIS CAUSED BY THE PROTEUS VULGARIS.

By Simon Flexner, M. D., *Associate in Pathology.*

(*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*)

Hauser, in 1885, isolated from putrefying animal substances the proteus group of micro-organisms, and these possessed the property of setting up putrefactive decomposition when added in pure culture to sterilized or non-sterilized meat. A number of instances have been published since which tend to show that the proteus bacteria may exert pathogenic effects on human beings.

Foà and Bonome found in the blood and organs of a man dead of supposed volvulus with hemorrhagic infarction of the intestine and mesentery and thrombosis of the mesenteric vein, a bacillus which they identified as the proteus vulgaris.

Hlava found the same organism in a case of "hemorrhagic infection," but he regarded it as accidental and ascribed no pathogenic effects to it.

Hauser described a case of phlegmonous inflammation of the hand and forearm from which he obtained both proteus and streptococcus. He considers that an actual symbiosis exists between the two bacteria, and thinks the necrosis of tissue caused by the streptococcus enabled the proteus to grow, while the effect of the latter in diminishing the tissue resistance permitted the streptococcus to invade more readily.

Proteus has been found in the intestinal canal of infants suffering from summer diarrhœa, by Booker and by Baginsky, and it is regarded as being of pathological significance.

The recent work of Jaeger, if confirmed, proves that the proteus organisms possess marked pathogenic properties. He studied a series of cases of Weil's disease which occurred in the garrison at Ulm. His investigation comprised eight cases, two of which came to autopsy. The remaining six were studied during life, cultures being made from the blood and urine.

In the two cases which were examined at autopsy no organisms were found in cover-slip preparations from the organs. But agar-agar, gelatine and bouillon cultures from the liver, kidneys, spleen and medulla oblongata of the first one, and liver, spleen and kidneys from the second, gave positive results. The organisms cultivated from these sources were identified with the proteus group. Examination of sections, stained in Kühne's methylene-blue, gave positive results. As a rule the organisms were more difficult to demonstrate in the kidneys than in the other organs, but when found they were often present in surprising numbers.

The blood of the six cases gave negative results, while the urine, drawn into sterilized Erlenmeyer's flasks after thorough cleansing and disinfection of the penis, gave in cover-slip preparations a positive result in every case. Cultures made from the urine were successful in four of the six cases. The organisms obtained were identified with proteus.

Babes reports the case of a boy 13 years old who exhibited uræmic symptoms and diarrhœa, and at the autopsy was found to have cirrhosis of the liver, hydronephrosis and extensive diphtheritic necrosis of the mucous membrane of the large intestine. From the organs of this case he obtained a bacillus which he regarded as proteus vulgaris.

The case of proteus infection which we observed was that of a young woman aged 18, white, who was admitted into the service of Dr. Osler, Johns Hopkins Hospital, on October 29th, 1892, and died on October 31st. When admitted, she was irrational and answered questions in a confused way. She complained of pain in the abdomen. No history could be obtained.

Status præsens. She has some twitching of the extremities. She slept well during the first part of the night, but after that was restless; this morning she vomited. Face rather flushed; eyes bright; lips and mucous membranes good color; pupils react to light. Chest well formed; percussion note clear in front and back; respirations clear in front and right back; a few sibilant râles heard over left back. Heart dulness somewhat increased to left. Apex beat to left of nipple line and forcible. Sounds are clear. Second pulmonic somewhat louder than second aortic. Pulse regular, 72. Abdomen is prominent in hypogastric and lower umbilical regions; wall held quite tense; right flank is slightly duller than left on percussion and more painful on deep palpation; otherwise negative. Spleen not palpable. Urine, drawn by means of catheter, light yellow in color, alkaline in reaction, specific gravity 1011, contains much albumen, some red blood corpuscles, small number of pus cells, a little epithelium of transitional variety, but no casts. The specimen was centrifugalized.

Autopsy 12 hours after death. Anatomical diagnosis:

Chronic diffuse nephritis (contracted kidney); slight heart hypertrophy; sero-fibrinous peritonitis; acute pleuritis; chronic pleuritis; pyosalpinx; swelling of follicles of intestine; single tuberculous ulcer of small intestine; chronic passive congestion and cloudy swelling of liver. Only such portions of the autopsy report will be given as bear on the present aspect of the case.

Peritoneal cavity.—In the dependent portion about 300 ccm. of faintly turbid serum containing flakes of fibrin. The peritoneum is congested, the vessels bright red and turgid, and small punctiform hemorrhages are visible beneath the peritoneal coat. Over the general visceral peritoneum there is a fine granular deposit of fibrin, which, on removal, leaves the underlying coat of the intestine free from gloss and vividly injected. Between the loops of the ileum, in the pelvis, are masses of fibrin easily removed by scraping with the finger. Over the stomach, spleen, liver, and on the under surface of the diaphragm is a similar thin fibrinous layer easily removable. The omentum is brightly injected. The body of the uterus is covered with a fibrinous membrane; on the ovaries, tubes and peritoneum covering the rectum are similar masses of fibrin, and in the latter larger hemorrhages exist.

Pleural cavity.—There is no excess of fluid in either. The lower lobe of left lung is covered by a fresh fibrinous deposit, and the same kind of membrane covers the pleural side of the diaphragm. No acute pneumonia.

Kidneys.—Combined weight, 155 grams. Dimensions, 9 × 5 × 2 cm. Average thickness of cortex, 4 mm. The capsule strips off with comparative ease, the surface is mottled and quite coarsely granular. On section the cortex is pale, the striæ obscure. The glomeruli are apparently diminished in number, but red. The cortex presents an opaque yellowish tint; the pyramids are darker in color than the cortex. Frozen sections show a great diminution in the number of uriniferous tubules and glomeruli in the specimens, and a corresponding increase in the amount of intertubular tissue. The epithelium of the remaining convoluted tubules is quite fatty; and fat is also present in the glomeruli and newly-formed connective tissue. Many dense, hyaline casts are seen in the collecting tubules. There is an extensive obliterating endarteritis.

Intestine.—Just above the valve the Peyer's patches are swollen and congested, and an irregular ulceration 7.5 mm. in length exists at this place. The loss of substance does not extend beneath the submucosa. The solitary follicles of the small intestine are somewhat swollen. On microscopical examination the ulcer proves to be tuberculous. The base of the ulcer is covered with granulation tissue.

Bacteriological examination.—Cover-slip preparations made from the peritoneal exudate showed large bacilli only. From the organs negative. Cultures were made in agar-agar and gelatine from the peritoneal exudate in the pelvis, the peritoneum covering the diaphragm; the liver, spleen, kidneys and lungs. No growth was obtained from either the liver or spleen.

Peritoneal cavity.—The gelatine roll tubes from the pelvis contained after 24 hours in the thermostat a large number of small colonies; from the diaphragm similar but fewer colonies. Within the next 24 hours the former tube had run down, and in the latter the colonies had enlarged and now presented the characteristic swarming appearance of proteus colonies. Cover-slips from both tubes gave the same organisms: bacilli, with rounded ends, varying in size, and forms which resemble cocci. Slanting agar tubes were inoculated from a single colony from each of these sources. A grayish white carpet was obtained on the surface of the agar from each.

From these agar tubes dated November 3, 1892, gelatine Esmarch tubes were made on January 3, 1893. The agar tubes had dried down considerably, but the growth still seemed to be pure. These gelatine rolls were placed in the thermostat at 22° C. After 24 hours the series (three in number) from the pelvic peritoneal growth on agar, gave the following results: First tube very cloudy; there are large liquefying colonies on the surface and the tube is already beginning to run down. Under the low power of the microscope (Leitz No. 3 objective) many small colonies are visible in the depth of the medium causing the cloudy appearance mentioned. The second tube contains fewer liquefying colonies; these have the size of a pin's head. Under the low power they are granular, quite circular in outline, and no projections are seen. Many small microscopic colonies also present. From the growth on agar from the diaphragmatic peritoneum a similar set of gelatine rolls was prepared. The growth here was a little slower and liquefaction less advanced than in the previous instance. Cover-slips from both sources show, however, the same bacteria to be present and these correspond with those previously described.

Hanging drop.—A single colony was examined and the organisms showed considerable motility. The rods looked a little longer and not quite so thick as in the carbol-fuchsin stained specimen. The motion is either a swimming, side to side movement, or a rolling and tumbling one. Not all the bacteria were equally active, and some exhibited only the Brownian movement. The coccus-like forms presented a rapid, dancing movement. A large bacillus, 2 to 3 times the average length, with more sluggish movements, was observed. On January 5th the entire set of tubes had run down, and gelatine stab cultures from single colonies on these had, in 24 hours in the thermostat, grown out and a cup-like depression of liquefaction already made its appearance. Twenty-four hours later the liquefaction of the gelatine had progressed from above downwards so as to take in about half of the medium.

Milk.—January 8th two milk tubes, one plain and one with litmus, were made from the 24-hour old stab on gelatine from the peritoneum. Twenty-four hours later, the tubes having been kept at 37° C., the litmus milk was changed from pale blue to pink, but no coagulation had taken place. The plain milk was unchanged. After 48 hours the milk was still uncoagulated. The tubes were then removed from the thermostat and kept at the room temperature. They were not closely watched, and when looked at several weeks later both had coagulated, with an abundant separation of serum. The pink color of the litmus milk persisted.

Potato.—The surface growth after 48 hours was slight; but a more considerable growth had taken place in the fluid at the bottom of the tube. Cover-slips from the surface showed

chiefly bacilli. They stained irregularly, and sometimes they were much distorted, evidently in process of involution.

Kidney.—A set of Esmarch roll tubes was prepared in gelatine from the original agar tube made at the autopsy. Placed in the thermostat at 22° C., tube number one was diffusely cloudy after 24 hours, and some large colonies were visible on the surface surrounded by a zone of liquefaction. Cover-slips showed bacillus and coccus forms, and a few of the bacilli were longer than the majority, equaling in length at times 4 to 6 of the average size. *In hanging drop* the motility resembled that described in the peritoneal tube. After 48 hours all the tubes had run down. A gelatine stab culture behaved in the same manner as those prepared from the peritoneal tubes. Transplantation to milk gave, after 48 hours, complete decolorization of the litmus, with the exception of a line corresponding with the separation of the cream where a pink color persisted. The milk was coagulated, with separation of serum. The plain milk tube was coagulated likewise.—*Potato.* After 24 hours there was a growth along the needle track, which after another day had increased. The color of the growth was grayish white. Cover-slips from this growth showed bacillus and coccus forms of micro-organisms, with the same variation in staining properties as has been mentioned in connection with the peritoneal potato growth.

Lung.—Gelatine Esmarch rolls show large colonies on the surface and smaller ones in the depth. The surface colonies were bluish in color, the margins serrated, and the whole colony seemed to project into the lumen of the tube. No tendency to liquefaction. Cover-slips from the two kinds of colonies show the same organisms: short, plump bacilli with rounded ends, 2 or 3 times as long as broad, with an occasional longer bacillus equal to 2 or 3 of the average size. Very seldom the bacilli were observed to be in pairs. Transplanted to *milk*, after 24 hours at 37° C. the plain milk apparently was unaltered; the litmus milk had assumed a pink color. After 48 hours both tubes were thickened, but no actual separation of serum had taken place. Removed from the thermostat and allowed to remain at the room temperature, after 8 hours the plain milk showed a beginning separation of serum, but the coagulum was finely subdivided. Less tendency to separation was manifested by the litmus milk. The tubes were not closely watched, but after several weeks at the room temperature they were again examined and the plain milk had coagulated firmly, the litmus milk somewhat less. On *potato* an abundant yellow growth was obtained.

We are, therefore, able to separate the organism found in the lung from those in the peritoneal cavity and kidneys. The first agrees with the bacillus coli communis, and as we have often found the colon bacillus in the lung in human beings dead of a variety of causes, we have no doubt as to its identity. The organisms from the peritoneal cavity and kidneys agree with each other in all essential particulars. It is worthy of note, however, that such a difference in the coagulating effect on milk exists, and this is of interest in connection with the known variation in the effect of the organism on gelatine. From the morphology and such of the biological properties of the organisms as we studied, it seems clear that they belong to the proteus group.

A word should, perhaps, be said with reference to the probability of the proteus having been a secondary invader, possibly post-mortem. We think that this supposition can be safely rejected. Although according to Bordoni-Uffreduzzi the proteus is the predominating post-mortem organism found in the tissues and blood of man and animals 24 to 48 hours after death, yet our experience has been far different. It is our rule to make cultures from all autopsies, and the proteus occurs rarely. Moreover, this autopsy was made in cold weather, soon after death, and no signs whatever of decomposition were present.

With reference to the pathogenic effects of proteus in this case there can be little doubt. An extensive peritonitis existed, and a single kind of organism was present in the exudate. Yet it must be considered that the natural properties of the proteus group of organisms are probably not such as to make them pathogenic for man under normal conditions. Hence it is of interest to consider just what the conditions may be in which they are enabled to exhibit such marked pathogenic properties as those mentioned. The proteus is a widely diffused organism in nature. It is found in the intestinal canal of human beings, and doubtless under ordinary conditions of health it might find its way into the peritoneal cavity without doing any great damage. But the conditions are greatly changed in such a case as this one. Here we have a system rendered particularly vulnerable to the invasion of bacteria in consequence of an extensive chronic disease. Cases somewhat similar are not rare. The terminal inflammations of serous membranes associated with long-standing renal and hepatic disease are well known. But it is of especial interest to know that organisms which do not exhibit under ordinary circumstances any especial pathogenic properties in human beings, may, in the altered state of the fluids of the body caused by these diseases, produce definite and wide-spread pathological lesions.[1]

The present case furnishes an illustration in the existence of a chronic nephritis; and as an especial predisposing cause the ulcer of the intestine permitting a more ready ingress to the peritoneum from the intestine should be considered.

With reference to the classification of the several species of proteus originally described, Hauser now thinks that such a separation as first proposed is not justifiable. The distinction based on the liquefaction of gelatine has been found to be insufficient to distinguish the several kinds, for in the case of a specimen of P. Zenkeri which had during 60 generations not liquefied gelatine, the 61st generation caused its liquefaction. Hence he now regards the several species originally made as varieties of proteus vulgaris.

Kuhn had previously come to the conclusion that P. mirabilis could not be considered a distinct species, but still adhered to the difference between P. vulgaris and P. Zenkeri.

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NOTE ON THE INCREASE IN THE NUMBER OF THE LEUCOCYTES IN THE BLOOD AFTER COLD BATHS.

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In the Centralblatt für Klinische Medicin for March 4, 1893, Prof. Winternitz of Vienna makes a communication concerning "Leucocytosis following Application of Cold."

He finds that in normal individuals as well as in cases of fever an appreciable leucocytosis is found as early as half an hour after the exposure to cold. In some cases he found that this lasted as long as two hours.

He calls attention to the recognized fact that the mere reduction of the temperature cannot of itself account for the many good effects of the treatment of fevers by cold baths, and he refers to the interesting experiments of Roque and Weill,[1] who showed that in typhoid fever treated with cold bathing the "urotoxic coefficient" was increased to from six to eight times its amount when the cases were treated by internal antipyretics or by other methods. He suggests that the application of cold calls forth in some way an increased number of leucocytes from the blood-forming organs into the blood current, where they probably exert a destructive influence on any pathogenic organisms which may obtain entry into the circulation. Some such process as this, he thinks, accounts possibly for the favorable influence of cold in the treatment of various infectious diseases.

The appearance of this note may justifiy a preliminary communication concerning some unfinished observations which have been made during the last six months in Prof. Osler's wards at the Johns Hopkins Hospital.

Last November Dr. J. S. Billings, Jr., called attention to the fact that in several cases of typhoid fever in which he had been counting the blood, he had found a distinct increase in the number of the leucocytes following the cold baths. These counts Dr. Billings followed with others, and since then further observations have been made.

The leucocytes have been counted before and after baths in twenty cases of typhoid fever, in one case of acute pneumonia, and on two occasions in the healthy individual. The baths were all given at 70° F. and were of twenty minutes duration. The temperature of the water was kept constant by means of ice.

[1] Revue de Médecine, Sept. 1891.

The blood was taken from the lobe of the ear from cuts made by a small spear-pointed lancet. Care was taken in making the second count to avoid the region of the first cut, and in the later observations the blood was taken from different ears. The Thoma-Zeiss blood counter was used and the blood was diluted with Toison's solution. In the first eight counts the blood was diluted two hundred times, and four whole fields of the blood counter were counted; the mean was then taken. In the later counts six whole fields with a one to two hundred dilution were counted, or four with a one to one hundred dilution. With several blood counters—in some instances six were used—such a method is quite rapid and gives a fair estimate of the number of the corpuscles.

The results may be seen in the accompanying tables. In Table I it will be seen that in twenty observations in cases of typhoid fever there was an increase in the number of the leucocytes after bath in eighteen instances, while in two there was a slight diminution.

In the twenty cases the average number of leucocytes before the bath was 7724+; after the bath, 13,170+. In the first eight cases where the exact time at which the blood was taken was not noted the average increase in leucocytes was, it may be seen, much smaller than in the latter twelve. In the first eight cases the average number of leucocytes before and after the bath averaged respectively 8000 and 10,437; in the second twelve cases 7541 and 14,492. It may be possible that a somewhat longer time elapsed between the bath and the second examination in the first cases than in those which followed. In one instance a bath was given to a patient with acute pneumonia; here the blood showed little change. Following these two observations were made with the healthy individual.

The writer himself took a bath of exactly the same character as those given to the patients with typhoid fever, *i. e.* at 70° F., lasting twenty minutes. The results may be seen on the chart. In the second observation the bath was a trifle colder and the cyanosis and shivering were much more marked than in the first instance. It will be seen that while on the first occasion the number of leucocytes was but little influenced, in the second instance it was nearly quadrupled.

TABLE I.

A.—Blood in Cases of Typhoid Fever.

NUMBER.	DATE.	NAME.	LEUCOCYTES BEFORE BATH.	LEUCOCYTES AFTER BATH.	REMARKS.
1	6-11-92	M.	5,500	11,000	
2	29-11-92	do.	6,500	10,000	
3	6-11-92	M.	9,500	10,500	
4	15-11-92	H.	8,000	12,000	
5	16-11-92	W.	9,500	10,000	
6	20-11-92	do.	7,500	9,500	
7	16-11-92	N.	9,000	12,500	
8	20-11-92	Mc.	8,500	8,000	
9	31-12-92	B.	6,666	24,000	First count made at 10.45 a. m. Bath given at about 11. Second count at 11.40. Patient blue and cold—shivering.
10	5-1-93	do.	4,500	9,715	First count at 9.50 a. m. Second at 11.05 a. m. Bath 9.55–10.15 a. m.
11	27-1-93	H.	6,857	17,000	First count at 3.05 p. m. Bath 3.40–4.00 p. m. Second count at 4.10 p. m. Patient was cold and shivering.
12	29-1-93	do.	6,000	9,000	First count just before the bath at 12.20 p. m., second count at 1.15 p. m.
13	29-1-93	K.	8,000	18,000	First count 11 a. m. Second count 11.45 a. m., 10 minutes after bath.
14	29-1-93	do.	8,500	17,000	First count at 3 p. m. Bath 3–3.20 p. m. Second count 3.30 p. m., 10 minutes after bath.
15	Date not recorded.	do.	10,284	16,000	First count at 3.45 p. m. Second at 4.15 p. m., just after the bath.
16	Date not recorded.	H.	5,500	13,000	First count at 5.10 p. m. Second count at 5.45 p. m.
17	4-2-92	A.	12,587	10,857	First count at 3.30 p. m. Second count at 4.30. Bath 3.40–4 p. m. Patient was warm and red. Red corpuscles { Before, 5,104,666 / After, 5,736,000 } mean of 3 counts of 200 squares each with $\frac{1}{210}$ dilution.
18	Date not recorded.	B.	10,600	19,000	First count at 11.25 a. m. Bath 11.40–12.01 p. m. Second count at 12.25 p. m.
19	23-3-93	do.	6,333	16,000	First count at 4.45 p. m. Bath 4.50–5.10. Second count at 5.40 p. m. Blood taken from different ears. Hands cold, ears bluish but warm. Red corpuscles { Before, 5,138,000 / After, 5,104,000 } mean of 3 counts of 200 squares each with $\frac{1}{210}$ dilution.
20	5-4-93	W.	4,666	10,333	First count at 9.10 a. m. Bath 9.17–9.37. Second count 9.47 a. m. Patient was not shivering, but ear was cold.
	Mean.....	.....	7,724 +	13,170 +	

B.—Acute Pneumonia.

1	16-2-93	R.	30,666	34,333	Blood taken at 3.45 p. m. Bath 4.15 p. m. Second count at 4.35 p. m., when patient was shivering but not blue. Red { 5,685,333 / 5,765,333 } mean of 3 counts of 200 squares each with $\frac{1}{210}$ dilution.

C.—Blood of Normal Individuals.

1		T.	10,333	12,333	First count made immediately before bath, which lasted 20 minutes. Second count 15 minutes after bath. Patient warm and red; no shivering.
2	16-4-93	T.	3,250	12,500	First count at 12 m. Bath 12.01–12.23. Second count at 12.25. Ear cold and slightly blue. Patient blue and shivering. At 12.40, when patient was still cold and shivering and ear cool, the count showed 10,250 leucocytes.

TABLE II.—DIFFERENTIAL COUNTS.

A.—Typhoid Fever.

NUMBER.	DATE.	NAME.	BEFORE BATH. Number of Leucocytes.	Lymphocytes.	Small Mononuclear.	Large Mononuclear.	Transitional (Indented Nuclei).	Multinuclear Neutrophiles.	Eosinophiles.	REMARKS.	AFTER BATH. Number of Leucocytes.	Lymphocytes.	Small Mononuclear.	Large Mononuclear.	Transitional (Indented Nuclei).	Multinuclear Neutrophiles.	Eosinophiles.	REMARKS.
1	31-12-92	B.	6,666	8.5		27.9	5.0	58.6			24,000	10.7		28.5	5.1	55.3		
2	27-1-93	H.	6,857	13.8		17.7	4.1	64,2			17,000	11.7		14.0	12.2	62.1		
3	29-1-93	do.	6,000	7.9		11.5	3.7	76.9			9,000	9.1		13.6	3.7	73.4		
4	23-3-93	B.	6,333	6.6	6.3	7.0	4.0	74.8	1.3		16,000	5.8	8.8	7.1	2.4	73.7	2.2	
5	5-4-93	W.	4,666	8.7	4.1	7.2	3.2	76.8			10,333	10.5	4.7	7.9	3.1	73.7	.1	

B.—Normal Blood.

1	16-4-93	T.	10,333	25.2	.3	1.8	4.9	59.0	8.8		12,333	25.0	.1	2.3	4.3	58.8	9.5	
2		T.	3,250	15.2	3.4	1.7	4.2	74.7	.8		12,500	15.5	3.3	1.5	3.0	74.8	1.9	

Thus it may be seen that in typhoid fever, at all events, cold baths are followed in most instances by a considerable increase in the number of the leucocytes; in some instances the number is increased nearly fourfold. And these, with the two counts in the healthy individual, would tend to fully confirm the observations of Winternitz.

The first suggestion which this discovery brought to mind —before any knowledge of the work of Winternitz—was that this marked increase in leucocytes might be in some way or other connected with the beneficial effects of the baths. But the extreme rapidity of the increase in the number of the leucocytes suggested also that the condition might be a local instead of a general one. Might it not be possible that the action of the cold in slowing the peripheral circulation should result in the accumulation of the leucocytes in the small peripheral vessels and capillaries? This question suggested a series of further observations which we hope to carry out, some of which are now in progress.

1. Assuming that we have in the leucocytes of the blood, elements in different stages of development, we might justly expect that if this increase in their number occurring in so short a time were actual, we should find some changes in the relative proportion of the different varieties of leucocytes one to another. Careful differential counts of the leucocytes were therefore made in dried and stained specimens made at the time of counting before and after the bath. It will be seen from the accompanying Table II that such have been made five times in cases of typhoid fever and twice in normal blood. These counts were made in specimens stained with Ehrlich's triple stain of acid fuchsin, methyl green and orange G. The particular mixture used in staining these specimens was made as follows:

Acid fuchsin saturated aqueous solution,	9
Water (distilled), ...	6
Orange G. saturated aqueous solution,	18
Methyl green " " "	20
Alcohol, ...	15
Water, ...	30
Glycerine, ...	5

To this several cc. of the saturated aqueous solution of methyl green were added, as the stain was not quite deep enough. The specimens were heated on the copper plate at 100°–120° C. for from one to two hours and were stained from two to five minutes. The classification adopted is essentially that of Tchistowitch,[1] excepting that the large and small lymphocytes are classed together, and that the large mononuclear forms with indented nuclei are classed as transitional forms. Several specimens were used, and at least one thousand leucocytes were counted in each instance.

The increased relative proportion of the large mononuclear and transitional (indented nuclei) forms in the blood of the typhoid fever cases will be noted, points to which Uskow[2] and Chetagurow[3] have called attention.

[1] Berliner klin. Woch. 1891, No. 34.
[2] "The Blood as a Tissue," St. Petersburg, 1890.
[3] Virch. Archiv, Bd. 120, F. XII, B. VII, 187.

It will be seen from the tables that the differences in the counts before and after baths have been very slight. In the five counts in the cases of typhoid fever there has, however, been one constant change, namely, a slight diminution in the multinuclear neutrophiles with a slight increase in the mononuclear forms. In cases 1, 3, 4, and 5 the increase appeared mainly in the lymphocytes and small mononuclear forms. In case 2 there was a diminution in the lymphocytes and small mononuclear forms, with an increase in the large mononuclear and transitional forms. In one case in which a count was made, but was not recorded in the list because of imperfections in the specimens from which the estimations were made, the opposite occurred, *i. e.* there was an increase in the multinuclear neutrophiles after the bath.

In the two instances in which estimates were made in the blood of a healthy individual the similarity between the counts before and after the baths is remarkable; there is practically no change whatever. This is all the more striking in the second instance where the increase in the number of the leucocytes was nearly fourfold.

So far then as we have gone the differences in the relative proportion of the different varieties of leucocytes one to another before and after the baths would appear to be only slight, if indeed they are appreciable.

2. Do those cases in which the bath is followed by an immediate reaction give the same results as those where there is cyanosis and coldness?

This question cannot yet be satisfactorily answered, but it will be observed that in case 17 of the typhoid fever cases, one of the two instances in which there was no increase in the number of leucocytes after the bath, the absence of cyanosis and chilliness was noted, while in the case of the writer the blood after his first bath, where there was an immediate reaction, showed but little change. On the second occasion, however, when there was shivering and cyanosis and the ear was blue and cold, the leucocytes were increased nearly fourfold. In case 9 of the typhoid fever cases where the greatest number of leucocytes was found after the bath, it was also noted that the patient was blue, cold and shivering. This was also noted in case 12 where there was a marked increase in the number of leucocytes. Cyanosis or coldness was also noticed is cases 19 and 20, where there was a considerable increase in the number of colorless corpuscles.

3. In any given case does blood from parts which are cold and blue show the same conditions as that taken from parts which are warm and red? This point has not yet been properly studied.

4. Does blood from a superficial cut with a lancet show the same condition as that from a deep needle prick or possibly from a larger vein? This point also has not been determined.

5. Do local applications of cold bring about the same result in the part as the more general baths? This important point we are not yet prepared to answer. It may be said that on two occasions the arm of a healthy individual was immersed in ice-water for a half an hour and the blood from a finger-tip counted before and after. In the first instance there were before the bath 7333 leucocytes in the cubic millimetre: immediately after a bath of 35 minutes, 9666. On a second

occasion there were 12,000 leucocytes before the bath, 10,666 immediately after, and 14,666 eighteen minutes later.

6. How soon does the increase in the number of leucocytes appear and what is its course? One can only yet say that a marked increase has been noticed inside of a half an hour after the beginning of a bath and also a half an hour or more after the bath.

8. Is there any change in the number of the red corpuscles in the cubic millimetre? In two of the cases of typhoid fever the red corpuscles were also counted. In one—case 17—there was an increase, while in case 19 there was a slight diminution noted. In the case of pneumonia there was a slight increase in the number of the red corpuscles. From this it would appear that there is no great constant change.

In conclusion, then, it is clear that in most cases prolonged cold baths are followed by a marked and rapidly appearing increase in the number of leucocytes in the blood obtained according to the ordinary methods of clinical examination. The question, however, as to whether this increase is general throughout the circulating blood or whether it is only local, due to the accumulation of leucocytes in the smaller peripheral vessels, is not so easily determined and requires further investigation.

From the results of the differential counts which have been made, and from the few observations concerning the condition of the peripheral circulation in the cases in which examinations of the blood have been made, one would perhaps be rather inclined to expect that further observations would tend to show that the increase in leucocytes following cold baths is more a local than a general condition.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Meeting of January 16, 1893.—(*Continued.*)

A Case of Chronic Aggravated Gout.—Dr. Hewetson.

This patient, aged 70, a contractor, came to the outdoor department on the 17th of November, complaining of swelling in various joints of his hands and feet, associated with a great deal of pain, which was much increased by motion and especially interfered with walking. There is no history of gout or of any other inherited disease in the family. He was born in this country and, with the exception of malarial fever, was always very healthy until he went to South America as a young man. While there he had some acute fever lasting ten days, the nature of which is not known. He also admits drinking to excess, using ale chiefly, but also the stronger alcoholic drinks. Since that time he has taken whiskey freely, but never, he says, to excess. He admits gonorrhœa, but denies syphilis.

This present illness began twenty years ago with an attack of what was thought to be rheumatism. The metatarso-phalangeal joint of the right big toe first became swollen, red, and extremely painful; this latter feature being especially marked at night. After a few days the same joint in the left foot became affected, and subsequently nearly all the joints in both feet. Altogether he was confined to bed for four weeks during this first attack, after which he remained comparatively well for ten years, suffering only from slight twinges from time to time. This second seizure was, however, more severe and the patient was obliged to remain in bed for four months, suffering acutely, as on this occasion nearly all the joints were involved, and especially those of the hands and feet. These latter have since that time remained swollen and distorted, if anything becoming larger, he thinks, with each subsequent attack, of which several occur during each year.

Walking has, for some time, caused great pain, and his fingers have become so stiffened that he can scarcely button his coat. A short time ago one of the nodules on his foot broke open and a white putty-like substance escaped, and on prying out one which had for some time projected through the skin of his finger, he was able to write with it upon a blackboard as well as if it had been chalk. During each attack he suffers from dyspeptic symptoms and has noticed his urine to be high-colored, but has never complained of hoarseness, asthma, neuralgia or of any of the other symptoms often associated with gout.

The physical examination shows a pulse of high tension, thickened arteries, an hypertrophied heart with a sharply accentuated aortic second sound, and evidences of emphysema, together with the deformities of the hands and feet of which he complains. These exist chiefly about the joints, and especially about the smaller ones, as can be seen. The skin over the hands and feet is usually cyanosed, so that the yellowish white tophi show clearly through the thin layer stretched over them. Some of these are soft and have a putty-like feel, others are firm and hard. They have caused much enlargement and deformity, and, in most of the joints of the fingers, loss of motion. A scar marks the spot where the chalk-stone was removed from the finger, and a fibrous sac remains where the one was discharged from the foot.

There are two small tophi to be seen in the cartilage of the left ear.

Just under the skin below the left elbow a group of eight or nine fibroid masses can be felt, which Dr. Osler thinks are the subcutaneous fibroid nodules of rheumatism, as no chalky deposit can be felt in them.

Urine is pale, of low specific gravity, and contains a faint trace of albumen with tube casts.

He has tried many remedies, but finds that wine of colchicum gives him the greatest relief during the attacks. In this case alcohol seems to have been the chief etiological factor, and we have a history of many acute attacks followed by this chronic condition, which is associated with cardio-vascular changes.

The term aggravated would not, perhaps, be used in Europe as applied to this case, but the rarity of gout in this country and its comparative mildness possibly renders it admissible for us now.

Advancement of the Internal Rectus.—Dr. Randolph.

This is a case of divergent squint upon which I operated some weeks ago. Cases of squint are, of course, familiar sights to us all, but in by far the majority of cases they are of the convergent variety, and are generally easily remedied by simple section of the internus of the affected eye or of both interni. Divergent squint in 60 per cent of cases is associated with progressive myopia and is more often seen at the beginning of adult life, and when so met with is the result of a process which has gone on for years and which has brought about a lengthening and thinning of the internal rectus muscle and a corresponding shortening and hypertrophy of the external rectus. Simple section, then, of the external rectus will not be followed by relief from the divergence. In such cases, for example as this one, there will be scarcely any difference in the deformity after section of the external rectus. Owing to the increased length of the internal rectus and to its long period of inactivity it is unable to do its work and the eye still diverges. In these cases we must resort to advancement, an operation first practised by Jules Guerin, and afterwards modified by von Graefe.

The operation here consisted in making a free tenotomy of the external rectus, and severing the internal rectus from its insertion, cutting out a section, or, in other words, shortening it, and bringing it forward and attaching it with three sutures at the border of the cornea. It is well to attempt to produce at the operation a little over-correction, in other words, slight convergence, as there will be a tendency to outward deviation during recovery. There is no operation in eye-surgery which is attended with more unsatisfactory results than the operation of advancement. In so many cases no good comes of it; in fact, the different steps of the operation are not such as can be taken with the same degree of definiteness as many of the other eye operations. On account of the generally unsatisfactory results of the operation, then, have I presented this case this evening. He was operated upon three weeks ago, and, as you will observe, his eyes are absolutely straight.

I may say here that the divergence in this case is not associated with myopia. In fact, I am led to believe that it is due in some way to imperfect innervation of the interni, arising from brain trouble in childhood. He gives a history of having had "brain fever" as a lad. He is now 26 years old and is far below the standard mentally.

Cases of Dilatation of the Colon in Young Children.—Dr. OSLER.

Dr. Osler remarked that a moderate grade of dilatation of the colon, by no means an uncommon condition, occurs at various periods of life, most commonly associated with chronic constipation. There are, in addition, instances on record of unusually great dilatation, either of the entire large bowel or of the sigmoid flexure; thus in the Index Catalogue there are twelve references to cases of dilatation and hypertrophy of the colon. The most extraordinary instance on record is that recorded recently by Dr. Formad:* the case of the museum *freak* known as the *balloon-man* or the *windbag*. This individual, aged at the time of his death twenty-three years, had been of a constipated habit, and had had a distended abdomen ever since his earliest infancy. Post-mortem there was found to be no obstruction; the colon was as large as that of an ox, the circumference ranging from 15 to 30 inches. Its weight, with the contents, was about forty-seven pounds.

One can readily understand dilatation and hypertrophy of the colon being gradually induced in consequence of protracted constipation, but there are instances in which, apparently from the earliest period of life, the large bowel is inert, and in which there would appear to be a tendency to dilatation without any protracted impaction of fæces. The following cases are of interest in this connection:

Case I.—John T. W., colored, aged ten, was admitted to Ward F of the Johns Hopkins Hospital, Feb. 17, 1892, complaining of a swollen and painful abdomen. The boy was brought to the hospital by his relatives, who live outside the city, and as they were not seen by the attending physician, no history could be obtained. It is stated, however, that he had, for many years, trouble with his bowels and had always had a large, prominent abdomen.

Present condition: Sparely built, somewhat emaciated lad, weighing only forty-seven and a half pounds; lips and mucous membranes of good color. The ends of the bones are not enlarged and he is not bowlegged. He is able to walk about, but the abdomen looks distended and large. There is no fever; the pulse is quiet. When stripped the contrast between the distended paunch and the thin emaciated limbs is very striking.

The thorax is symmetrical, and the lower zone is much distended by the enlarged abdomen. The ribs are little beaded. The back shows several reddish, superficial scars where the child has been beaten. The heart impulse cannot be distinctly localized, but is apparently under the fifth rib and a little inside the nipple line. The sounds are clear; the second a little accentuated. The examination of the lungs is negative.

The abdomen is greatly distended, measuring 63 cm. just above the navel. It is uniform, on palpation tense, painless, and no tumor masses can be felt. Percussion gives everywhere a tympanitic note. The spleen is not palpable, and the splenic dulness is masked by the tympany. The edge of the liver cannot be felt, and dulness is obliterated in the middle parasternal and nipple lines.

The urine was normal.

Nothing very definite was determined at first about the nature of the lad's illness. There was certainly neither ascites nor tumor, and the suggestion that it might be tabes mesenterica was negatived. The child was kept in bed and given a good diet. The first and second day in hospital he had an ordinary movement from the bowels, not specially constipated.

On the 22d he had diarrhœa, six large liquid movements. On the 23d and 24th there was only one movement on each day, and then for three days he was constipated. Repeated examinations showed practically the same condition: enormous abdominal distension without any obvious cause. He complained of no pain, and we very soon let him go about the ward. At intervals he would be constipated, but this was readily relieved by a dose of castor oil, and never during the months of February and March did he go for more than two days without a movement. On several occasions he had, even without castor oil, loose fluid motions. All this time he had no fever, and was up and about the ward and gained four pounds in weight.

On the night of the 23d the patient had four loose fluid movements and complained of abdominal pain. On the morning of the 24th he vomited several times, and the abdomen seemed more distended, and the contractions of the intestinal coils were very plainly to be seen. On the night of the 24th he was given several large injections which brought away formed masses of fæces. The abdomen measured in its largest area 74 cm.; was tympanitic throughout; not very tender on pressure. The individual coils during peristalsis stand out very plainly. The outline of the colon could be distinctly seen, extending obliquely from the left lumbar region to the tip of the xiphoid cartilage. The examination externally and per rectum could determine no tumor. No flatus could be obtained with the rectal tube passed high up, but relief was obtained by introducing the tube far up and irrigating the bowel thoroughly, and with this a large quantity of fluid came away. The distension persisted throughout the 25th and 26th and 27th; the vomiting, however, was less and the injections gave relief. The tenderness was less, and the distension of the abdomen was not so marked, being only 69.5 cm. on the morning of the 27th. He was very much better the next day, but on the 29th he developed facial erysipelas and was transferred to the infectious ward. Here the erysipelas ran a regular course, with very moderate and irregular fever, which persisted with intermissions until the 10th. When in the isolating ward the abdomen was not so distended; he had several attacks of constipation, but the bowels were readily moved by laxatives. During this time he had also several attacks in which there was great pain in the abdomen with increase in distension, and at this time the coils of the intestine became very marked. He was in the isolating ward for about ten days, and after his return to Ward F the abdomen was very large, measuring sometimes as much as 80 cm. in circumference, and he had several attacks of pain and vomiting. At no time in these vomiting attacks was the material brought up fæcal in character. They were always relieved by the high enemata, which were given with the hips well elevated, and letting as much run in as possible from a height of six feet.

The increased frequency of these attacks of pain and vomiting made me feel that it would be advisable to have an exploratory operation in order to determine definitely whether there was

* University Medical Magazine, 1892.

any cause for the trouble, though it did not seem possible that there could be any obstruction, as the fluids passed so freely from the siphon syringe. Accordingly he was transferred to the surgical department on April 20th, and Dr. Halsted performed abdominal section. The following is an abstract of the notes from the surgical protocol:

Under ether a long incision was made in the median line, extending from a little below the ensiform cartilage to a little above the pubes. When the incision was completed an enormously enlarged colon rolled out upon the abdominal walls. The entire gut was enlarged. It was the greatest at the sigmoid flexure, where the measurement was exactly 45 cm. in circumference. The cæcum was about half this size, and the bowel progressively increased in diameter in the ascending, transverse, and descending portions. The sigmoid flexure was twisted on itself, but not so as to cause any obstruction. During the operation the rectum was thoroughly examined by Dr. Osler, whose finger could be readily felt by the hand of the operator, and no stricture could be determined anywhere. A moderate-sized fæcal mass existed in the rectum, not impacted, and after removal of this the tube was passed, but the distended colon did not empty itself through this. The small intestines were normal in size and appearance, and nearly empty. The intestines were wrapped in warm gauze, which was also packed around the incision.

Dr. Halsted then proceeded to make an artificial anus, opening the bowel at the most prominent part of the sigmoid flexure. A very large quantity of yellowish fluid fæcal matter escaped with gas. The muscular coats of the bowel were very much thickened; the mucous membrane seemed normal.

The boy did remarkably well and was sitting up in a chair on April 29th. His appetite and general condition improved; he gained in weight, and he had no further abdominal symptoms whatever. There was no tympanitis, and he passed the fæces through the artificial anus.

Unfortunately, we have not been able to obtain any account of the first years of this child's life, further than that he had always had a prominent abdomen and had trouble with the bowels. It may be, of course, that the enormous distension present when he came under our observation was only the sequence of protracted constipation, but, as mentioned in the history, there was not at any time during his stay in the hospital impaction of fæces, and the attacks of distension, colic and vomiting were, as a rule, readily relieved by simple injections, and at no time were hard, scybalous masses seen. The grade of dilatation in this case was extreme, a circumference of 45 cm. (about 18 inches), which equaled the circumference of the ascending colon in Dr. Formad's case. I must say that the attacks of vomiting, with increase in the distension, great tension of the abdominal walls, and visible coils in active peristalsis, excited the suspicion that possibly there was a stricture of some sort in the sigmoid flexure. It was for the purpose of exploring the large intestine that the laparotomy was performed. To have made an artificial anus in the case seems a serious measure, but the child's condition had become very distressing, and the rapid improvement which followed the operation is itself the best justification. Dr. Platt, under whose care the boy is at present, informs me that the boy's general condition is good, and that it is his intention to try to re-establish the continuity of the bowel.

Case II.—R. A., aged seven months, admitted June 12, 1891, with constipation. Father and mother are healthy and well. The first child, born November 20, 1889, natural labor. At about the seventh month the child had stomach trouble, continued diarrhœa, and died suddenly. The present is the third child. When born was a healthy, large child. It was noticed from the outset that the child's napkins were not soiled. The abdomen became swollen and very tense, but the doctor made an examination, passed a catheter, and the black, tar-like fæces were brought away. From the time of its birth the child has had only five or six natural evacuations. A careful examination of the rectum was made shortly after the child's birth, but no stricture was found, and large-sized dilators were passed easily. Sometimes the fæcal matter was hard and was with difficulty removed. In spite of this the child throve and seemed perfectly well, was well nourished, and did not cry or was not specially distressed so long as the bowels were thoroughly relieved every day by the injection. If not relieved the abdomen would swell and the child would vomit very much, at times large quantities of material which were sometimes bile-stained. Until two weeks ago the child seemed healthy and looked natural. At this time he began to be feverish, the gums were swollen, he cried a great deal, and had much vomiting when the bowels were not relieved, and the mother is sure there was a great deal of pain when the abdomen was distended. He has lost in weight and has not nursed well.

Present Condition.—Bright-looking child, moderately well nourished, rather small for its age; tongue is clean; no teeth as yet cut. The abdomen is greatly distended and very tense. The costal margins and the ensiform cartilage are strongly everted. The outlines of the coils of the intestines are distinct, particularly one very large coil passing transversely between the navel and the ensiform cartilage. There are no vermicular movements visible, but the mother states that they are often to be seen very plainly. On palpation the tension is considerable; there is no pain except on deep pressure; no fæcal masses; no tumor to be felt, but there is much gurgling of flatus. The liver dulness is almost obliterated; the spleen is not palpable. The examination of the rectum by the finger is negative. It did not seem to me that the sphincter was especially tight, but Dr. Halsted, who subsequently examined the child, thought it was a little more resistant and tighter than normal. A catheter is passed without any difficulty, and when it reaches a distance of eight inches much gas escapes, and if there has been a previous injection of water, fluid fæces. The usual routine the mother follows to relieve the bowels is to inject a few ounces of water an hour or two before she passes the catheter, which she then inserts to a distance of about six or seven inches, and gas and fæces come away. The abdomen becomes flat and soft at once after the escape of the flatus and fæces. The contrast between the tense, enormously distended abdomen in the morning after having been for twenty-four hours without an evacuation, and immediately after the use of the catheter, is very remarkable.

The patient was only under observation for about two weeks, and presented no change during this time. The distension did not seem to be due to obstruction, nor did it appear to be influenced at all by the use of free injections. The mother was advised to relieve the child's bowels with the catheter several times in the day, so as not to allow the flatus and fæces to distend the colon. The mother wrote seven or eight months after she left the hospital, saying that the child's condition remained practically the same.

Here we may possibly have an illustration of the early condition which leads ultimately to the enormous dilatation and hypertrophy met with in the last case and in the one reported by Formad. From birth there seems to have been an inability in the large bowel to empty itself, and this certainly was not, I think, associated with any degree of tightness of the sphincter, through which the index finger passed without difficulty.

Dr. Hurd.—It may be interesting to recall the fact that Schroeder Van der Kolk, in a paper on insanity written probably forty years ago, describes dilatation of the colon as of very frequent occurrence in cases of chronic insanity. In his autopsies he found it so frequently that he regarded it as one of the pathological conditions of chronic insanity. It would seem to indicate that in a great many of these cases there must be some inherent structural defect of the nervous system. I remember being very much struck with the large number of cases he reported. I do not know that any one else has ever seen a similar number.

Dr. OSLER.—I think the cases which are so common in asylums and almshouses are usually in old people who have chronic constipation and who suffer from attacks of fæcal impaction. I have seen enormous dilatation of the colon under such circumstances. But these cases do not seem to come under this category, because none of them seem to have had at any time fæcal impaction. There appears to be some defect of innervation in the colon, and probably in the contracting power of the muscles.

Catheterization of the Ureters, with Exploratory Nephrotomy. —Dr. STAVELY. See page 25, March BULLETIN.

Dr. OSLER.—I do not see why parasitic hemorrhage should not occur in this lady. It occurs in Charleston, and I think that if we look long enough we will find cases. Both of these cases are extremely interesting, demonstrating conclusively the fact that hemorrhage of some persistence may come from a single kidney, and may come without the presence of a calculus and without evidence of a neoplasm. I do not think that any incision of a kidney on the operating table could definitely exclude tuberculosis, for it would be quite impossible to examine all the infundibula and calices of the kidney, and we know that from quite a limited region in primary disease of the apex of a pyramid in tuberculous pyelonephritis hemorrhage may come and may persist for some time. Still I think there would have been more pus in the urine in these cases had they been tuberculous. There is a class of cases of hemorrhage without evident lesion and without any known etiology, cases which Gull very happily termed "renal epistaxis," as he said there was no more reason against a man bleeding occasionally from the mucous membrane of his kidney than from the mucous membrane of the nose.

It rather strikes the uneducated medical mind that for this condition so serious an operation as incision of the kidney might be of somewhat dubious propriety, but the results in these two cases justify the procedure. Surgeons do carve the kidney with remarkable impunity, and even for much less serious things than hemorrhage. We know that there have been a great many cases of operation for neuralgia. Dr. Tiffany of this city urges incision of the kidney substance for neuralgia of the organ.

Exhibition of Cases.—Dr. BALTZELL.

Laparotomy for Intussusception.—Dr. Baltzell exhibited two surgical cases for Dr. Halsted. The first case was a little baby of seven months who had come into the hospital six days before with an intussusception of the large intestine. The intestine protruded 34 cm. through the rectum. A laparotomy was done and the intussusception reduced. An umbilical hernia which was present was cured by the same operation. The child was doing nicely.

Subcutaneous Stitch.—The second case was exhibited as an example of the use of the continuous subcutaneous stitch. The operation was for the radical cure of hernia. It was done ten days previously and the wound was entirely healed. This suture brings the edges of the wound in close apposition. There are no knots in it, and at the end of two weeks it can be withdrawn entire by easy traction.

Arsenical Neuritis following the Use of Fowler's Solution. —Dr. OSLER.

On October 25th, 1892, the patient before you was admitted to my ward with Hodgkin's disease, the cervical, axillary, and inguinal groups being involved. Having had under observation for now nearly four years a case of this disease, which has been remarkably benefited by the prolonged use of Fowler's solution taken at intervals, we naturally placed this man upon the same drug. The details of his case, so far as they relate to the lymphatic disorder, do not concern us. The arsenic was begun on Oct. 27, given as Fowler's solution, and gradually increased. He took it on the first occasion for ten days; it was then resumed on Nov. 14, and in two weeks the dose reached 15 minims three times a day. Towards the end of November it was noted that his skin, which was naturally of a somewhat dark color, had a much deeper tint, and that of the abdomen was very distinctly bronzed. Throughout the month of December he did not do well. The arsenic was stopped on the 19th and begun again on the 27th. From the outset the patient has had that interesting feature in many cases of Hodgkin's disease, an intermittent pyrexia, and as may be seen by his last week's chart, the temperature rises every afternoon and evening to about 104°. The pigmentation seemed to increase throughout December. Twice during the first two months of his stay in hospital there was slight diarrhœa, which was attributed to the arsenic. About the middle of January it was noticed that he was tender to the touch and walked somewhat stiffly. He is a Pole, speaking no English, and as there was no one in the ward to interpret for him, these symptoms did not perhaps at first attract the attention they deserved. The most striking feature at this time was the sensitiveness on pressure. The skin itself did not appear to be painful, but if, for example, the arm was grasped, or the pectoral muscle lifted, or the thigh pinched, he winced and tears came into his eyes. By the end of January he walked with much difficulty and could scarcely go from his bed to the closet. He has naturally, in the course of his disease, wasted a good deal, but the legs seem to have become distinctly flabby within the past two or three weeks. The knee jerks, which were present on January 10th, are at present absent.

On February 2 Dr. Hoch reported the faradic excitability of the nerves of the leg was diminished, the galvanic also to a slight extent. In the muscles the diminution to both currents was more marked, and the contraction following the galvanic stimulation was decidedly slower, and the anode, if not larger, was at least equal to the K. C. C. The muscular power in the arm is not so strikingly diminished, though the grasp is feeble in comparison with what it was. The hypersensitiveness of the muscles does not appear to be at all diminished.

Between the 27th of October and the 10th of January this patient took ℥4 ℥1 ♏18 of the liquor potassi arsenitis, equivalent to 16¼ (ca) grains of arsenious acid. During these 75 days there were 14 days in which the drug was omitted. The marked sensory changes, the gradual impairment of muscular power, and the progressive character indicate very clearly the peripheral and neuritic nature of the affection, and though he has a chronic cachexia, in which, as in cancer or tuberculosis, peripheral neuritis might develop, yet it seems more rational to attribute it to the somewhat prolonged use of the arsenic, more particularly as he has had also another striking feature of arsenical poisoning, namely, pigmentation of the skin.

HOSPITAL HISTORICAL CLUB.

Meeting of February 13, 1893.

The following works were exhibited by Dr. Kelly to the Historical Club, February 13, 1893, from his private library, with comments upon the important periods in Vesalius's life in relation to his writings:

VESALIUS, Epistola [ad N. Florenati], docens venam axillarem dextri cubiti in dolore laterali secandam, et melancholicum succum ex venae portae ramis ad sedem pertinentibus purgari. Basileae, ex off. R. Winter. 1539. Small folio, one wood engraving. Calf. Very rare, first edition.

VESALIUS, De Humani Corporis Fabrica. Basileae, ex offic. J. Oporini. 1543. Reg. fol. Portr. and many wood engravings. Rare, first edition, parchment.

VESALIUS, Epistola Venetiis O. J. 1546. 8vo. Prgmtb. Rare, second print.

VESALIUS, Epistola [ad J. Rōlants], rationem propinandi radicis chynae decocti, quo nuper Carolus V. imp. usus est, pertractans, et praeter alia epistolae cujusdam ad J. Sylvium sententiam

recensens, hum. fabricae studiosis perutilem, quum qui hactenus in illa nimium Cl. Galeno creditum sit, commonstret. [ed. Franc. Vesalius frater.] Basileae ex off. J. Oporini. 1546. Small fol. with beautiful portrait in wood engraving after Titian's drawing, attributed to Joh. von Calcar. Parchment, rare first edition.

VESALIUS, Basileae, off. J. Oporini. 1555. Royal fol., with portrait in wood and numerous cuts. [Second and last author's edition.] ["Ed. plenissima et pulcherrima." J. F. Blumenbach.] Pressed hog's leather, with metal clasps.

VESALIUS, De Humani Corporis Fabrica Libri Septem. Per Joannem Oporinum. Handsome edition in calf. 1555.

VESALIUS, Epitome anatomica, cui accessere notae ac commentaria P. v. Paaw. Lugduni Bat. 1616. Small folio, copperplates, parchment.

VESALIUS, Epitome anatomica, c. acc. not. ac comment. P. Paaw. C. tabb. aen. Amst. 1633. Small quarto.

VESALIUS, Opera Omnia, anatomica et chirurgica. cur. H. Boerhaave et b. S. Albinus. 2 Tmi. Lugduni Bat. 1725. Reg. fol. with copperplates. Handsome title plate. Portr. [J. Wandelaar sc.], with 82 copperplates.

VESALIUS, Life by M. Roth. With 30 plates, pp. 500. Berlin, 1892.

Meeting of March 13, 1893.

Books exhibited by Dr. Kelly:

A clean, fresh, vellum-bound copy of Paul of Egina, Paris, 1532, f. ap. Simon Colinaeum. First edition of the translation by Guinter of Andernach, exceedingly valuable, prepared by study of original manuscripts.

Also the following books relating to various Hippocratic writings and teachings:

De Collectionis Hipprocraticae Auctorum Anatomia, August Hirsch, Berolini, 1864.

Materia Medica Hippocratis, Josephus Mendelius Raudnitz, Dresdae, 1843.

Hippocratis Coi Biologiae Explicatio Nova, Alexander Friedleben, Wirceburgi, 1842.

Hippocratis Magni Coi Opera Novo Ordine Digesta, Carolus Gulielmus Fickel, Zwiccaviae, 1833.

Ueber das Hippocratische erste Buch von der Diaet, Ernst Freiherrn von Fenchtersleben, Wien, 1835.

Discours sur le Genie d'Hippocrate, P. J. Barthez, à Montpellier, 1816.

Observationes de Usu Particularum in Libris qui Vulgo Hippocratis Nomine circumferuntur, H. Kuehlewein, Gottingae, 1870.

Die Chirurgie des Hypocrates, Joseph Fielder, Wuerzburg, 1868.

Du Buste d'Hippocrate, etc., H. Kuehnholtz, Montpellier, 1849.

Magni Hippocratis Secundi Vita et Scripta, Leopoldo Woerl, Friburgi Brisigaviae, 1835.

Vues Nouvelles sur la Chirurgie d'Hippocrate, J. G. Petrequin, Anvers, 1864.

THE JOHNS HOPKINS HOSPITAL REPORTS.

VOLUME I. This volume is now in press. It will contain the studies from the Pathological Laboratory. The volume will be provided with illustrations. It will be edited by Dr. W. H. WELCH, Professor of Pathology and Pathologist to the Hospital.

VOLUME II.—The second volume of the Hospital Reports began in January, 1890.

CONTENTS.

I. On Fever of Hepatic Origin, particularly the Intermittent Pyrexia associated with Gallstones. By WILLIAM OSLER, M. D.

II. Some Remarks on Anomalies of the Uvula, with special reference to Double Uvula. By JOHN N. MACKENZIE, M. D.

III. On Pyrodin. By H. A. LAFLEUR, M. D.

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